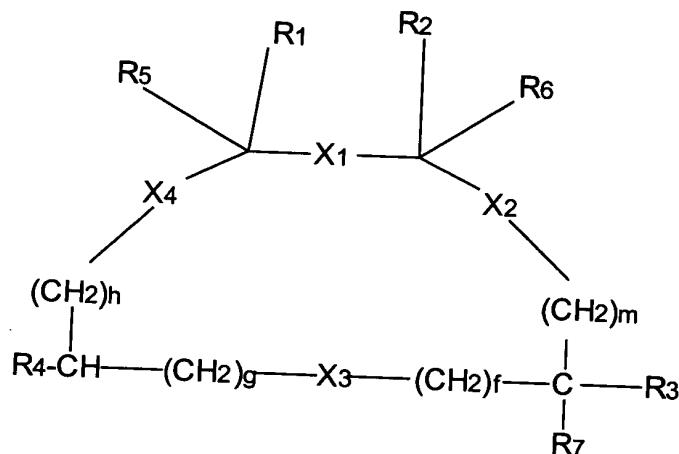


IN THE CLAIMS:

Kindly amend Claims 1, 3, 5, 8, 9 and 14 as follows:

PL  
1. (Amended three times) A monocyclic compound having the formula (1):



in which:

$X_1$ ,  $X_2$ ,  $X_3$ ,  $X_4$ , which may be the same or different from one another, is selected from the group consisting of  $-\text{CONR}-$ ,  $-\text{NRCO}-$ ,  $-\text{OCO}-$ ,  $-\text{COO}-$ ,  $-\text{CH}_2\text{NR}-$  and  $-\text{NR-CH}_2-$ , where R is H or a  $\text{C}_{1-3}$  alkyl or benzyl;

$f$ ,  $g$ ,  $h$ ,  $m$ , which may be the same or different from one another, may be 0 or 1;

$R_1$  and  $R_2$  which may be the same or different from one another, represent the side chain of a natural amino acid selected from the group consisting of tryptophan, phenylalanine, tyrosine and histidine, or the side chain

of a non-natural amino acid selected from the group consisting of:

tryptophan and phenylalanine, either mono- or di-substituted with residues selected from the group consisting of  $C_{1-3}$  alkyl or halo-alkyl,  $C_{1-3}$  alkoxy or amino-alkoxy, halogen, OH, NH<sub>2</sub> and NR<sub>13</sub>R<sub>14</sub>, where R<sub>13</sub> and R<sub>14</sub>, which may be the same or different from one another, represent a hydrogen or  $C_{1-3}$  alkyl group;

R<sub>3</sub> is selected from the group consisting of:

- linear or branched alkyl having the formula  $C_nH_{2n+1}$  with n=1-5 (selected from the group consisting of methyl, ethyl, propyl, isopropyl, n-butyl and t-butyl) cycloalkyl or alkylcycloalkyl of formula  $C_nH_{2n-1}$  with n=5-9 (selected from the group consisting of: cyclopentyl, cyclohexyl and methylcyclohexyl)

-  $(CH_2)_r-Ar_1$ , where r=1 or 2 and where Ar<sub>1</sub> is an aromatic group selected from the group consisting of:  $\alpha$ -naphthyl,  $\beta$ -naphthyl, phenyl, indole, said Ar<sub>1</sub> group being possibly substituted with a maximum of two residues selected from the group consisting of:  $C_{1-3}$  alkyl, CF<sub>3</sub>,  $C_{1-3}$  alkoxy, Cl, F, OH and NH<sub>2</sub>;

R<sub>4</sub> represents an L-Q group where:

L is a chemical bond of CH<sub>2</sub>, and

Q is selected from the group consisting of:

- OH, NH<sub>2</sub>, NR<sub>9</sub>R<sub>10</sub>, OR<sub>11</sub>, and where R<sub>9</sub> and R<sub>10</sub>, which may be the same or different from one another, represent a hydrogen or  $C_{1-3}$  alkyl group,  $C_{1-3}$ hydroxy alkyl,  $C_{1-3}$ dihydroxyaklyl,  $C_{1-3}$ alkyl-CONHR<sub>12</sub> (wherein R<sub>12</sub> is a monoglycosidic group derived from D or L pentoses or hexoses (selected from the group consisting of ribose, arabinose, glucose, galactose, fructose, glucosamine, galactosamine N-acetylglucosamine and

N-acetylgalactosamine)),  $C_{1-3}$ alkyltetrazole,  $C_{1-3}$ alkyl-COOH or wherein  $R_9R_{10}$  are joined together to form with the N atom a morpholine or a piperidine ring and where  $R_{11}$  is a  $C_{1-3}$  alkyl chain, or a  $C_{2-4}$  amino-alkyl chain;

*01*  
*Claims*  
NHCOR<sub>8</sub> wherein R<sub>8</sub> is a cyclohexane containing from 2 to 4 OH groups,  $C_{1-6}$  alkyl chain containing a polar group (chosen in the group consisting of NH<sub>2</sub>, COOH, CONHR<sub>12</sub>, (wherein R<sub>12</sub> is as hereabove defined) or [1,4']bipiperidine))

- COOH, COOR<sub>17</sub> or CONHR<sub>12</sub>, wherein R<sub>12</sub> is as hereabove defined and R<sub>17</sub> is as R<sub>12</sub> or a group 4-nitrobenzyl
- R<sub>5</sub>, R<sub>6</sub>, R<sub>7</sub> are H<sub>2</sub> in which the carbon atom that carries the substituents R<sub>3</sub> and R<sub>7</sub> has configuration R; wherein when R<sub>1</sub>=R<sub>2</sub>= a side chain of tryptophan and R<sub>4</sub>= CH<sub>2</sub>OH then R<sub>3</sub> is not isopropyl.

*03*  
3. (amended three times) A compound according to Claim 1 selected from:

- (a) Cyclo{-Suc-Trp-Phe- [(R) -NH-CH(CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>) -CH<sub>2</sub>-NH]}
- (b) Cyclo{-Suc-Trp-Phe- [(S) -NH-CH(CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>) -CH<sub>2</sub>-NH]}
- (c) Cyclo{-Suc-Trp-Phe- [(R) -NH-CH(CH<sub>2</sub>C<sub>6</sub>H<sub>11</sub>) -CH<sub>2</sub>-NH]}
- (d) Cyclo{-Suc-Trp-Phe- [(R) -NH-CH(CH<sub>2</sub>C<sub>6</sub>H<sub>4</sub>(4-OCH<sub>3</sub>) ) -CH<sub>2</sub>-NH]}
- (e) Cyclo{-Suc-Trp(5F)-Phe- [(R) - NH-CH(CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>) -CH<sub>2</sub>-NH]}
- (f) Cyclo{-Suc-Trp(Me)-Phe- [(R) - NH-CH(CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>) -CH<sub>2</sub>-NH]}
- (g) Cyclo{-Suc-Phe(3,4-Cl)-Phe- [(R) - NH-CH(CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>) -CH<sub>2</sub>-NH]}
- (h) Cyclo{-Suc-Trp-Phe(3,4-Cl)- [(R) - NH-CH(CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>) -CH<sub>2</sub>-NH]}
- (i) Cyclo{-Suc-Trp-Tyr- [(R) -NH-CH(CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>) -CH<sub>2</sub>-NH]}
- (j) Cyclo{-Suc-Trp-Phe- [(R) -NH-CH(CH<sub>2</sub>C<sub>6</sub>H<sub>3</sub>-3,4-diCl) -CH<sub>2</sub>-NH]}
- (k) Cyclo{-Suc-Trp-Phe- [(R) -NH-CH(CH<sub>2</sub>C<sub>6</sub>H<sub>4</sub>-4-OH) -CH<sub>2</sub>-NH]}
- (l) Cyclo{-Suc-Trp-Phe- [(R) -NH-CH(CH<sub>2</sub>-CH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>) -CH<sub>2</sub>-NH]}
- (m) Cyclo{-Suc-Trp-Phe- [(R) -NH-CH(CH<sub>2</sub>-2-naphthyl) -CH<sub>2</sub>-NH]}
- (n) Cyclo{-Suc-Trp-Phe- [(R) -NH-CH(CH<sub>2</sub>-indol-3-yl) -CH<sub>2</sub>-NH]}
- (o) Cyclo{-Suc-Trp-Phe- [(R) -NH-CH(CH<sub>2</sub>-5-F-indol-3-yl) -CH<sub>2</sub>-NH]}

(p) Cyclo{ -Suc-Trp-Phe- [(R)-NH-CH(CH<sub>2</sub>-C<sub>6</sub>H<sub>4</sub>-3-F)-CH<sub>2</sub>-NH] }

(q) Cyclo{ -Suc-Trp-Phe- [(R)-NH-CH(CH<sub>2</sub>-C<sub>6</sub>H<sub>3</sub>-3,4-diF-CH<sub>2</sub>-NH] - }

(r) Cyclo{ -Suc-Trp-Phe- [(R)-NH-CH(CH<sub>2</sub>-C<sub>6</sub>H<sub>4</sub>-4-CF<sub>3</sub>-CH<sub>2</sub>-NH] - }

(s) Cyclo{ -Suc-Trp-Phe- [(R)-NH-CH<sub>2</sub>-CH(CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>)-NH] }

(t) Cyclo{ -Suc-Trp-Phe- [(S)-NH-CH<sub>2</sub>-CH(CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>)-NH] }

(u) Cyclo{ -Trp-Phe- [(R)-NH-CH(CH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>)-CH<sub>2</sub>-NH] - (CH<sub>2</sub>)<sub>3</sub>CO- }

(v) Cyclo{ -Trp-Phe- [(R)-NH-CH(CH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>)-CH<sub>2</sub>-N(CH<sub>3</sub>)] - (CH<sub>2</sub>)<sub>3</sub>CO- }

(w) Cyclo{ -Suc[1(S)-NH<sub>2</sub>]-Trp-Phe- [(R)NH-CH(CH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>)-CH<sub>2</sub>NH] - }

(x) Cyclo{ -Suc[1(R)-NH<sub>2</sub>]-Trp-Phe- [(R)NH-CH(CH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>)-CH<sub>2</sub>NH] - }

(y) Cyclo{ -Suc[2(S)-NH<sub>2</sub>]-Trp-Phe- [(R)NH-CH(CH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>)-CH<sub>2</sub>NH] - }

(z) Cyclo{ -Suc[2(R)-NH<sub>2</sub>]-Trp-Phe- [(R)NH-CH(CH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>)-CH<sub>2</sub>NH] - }

(aa) Cyclo{ -Suc[1(S)-NH(CH<sub>3</sub>)]-Trp-Phe- [(R)NH-CH(CH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>)-CH<sub>2</sub>NH] - }

(ab) Cyclo{ -Suc[1-COO(CH<sub>2</sub>-C<sub>6</sub>H<sub>4</sub>-4-NO<sub>2</sub>)]-Trp-Phe- [(R)NH-CH(CH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>)-CH<sub>2</sub>NH] - }

(ac) Cyclo{ -Suc(1-COOH)-Trp-Phe- [(R)-NH-CH(CH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>)-CH<sub>2</sub>-NH] }
   
 [Cyclo{ -Suc(1-COOH)-Trp-Phe- [(R)-NH-CH(CH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>)-CH<sub>2</sub>-NH] }]

(ad) Cyclo{ -Suc(1-OH)-Trp-Phe- [(R)-NH-CH(CH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>)-CH<sub>2</sub>-NH] }

(ae) Cyclo{ -Suc(2-COOH)-Trp-Phe- [(R)-NH-CH(CH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>)-CH<sub>2</sub>-NH] }

(af) Cyclo{ -Suc(2-OH)-Trp-Phe- [(R)-NH-CH(CH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>)-CH<sub>2</sub>-NH] }

(ag) Cyclo{ -Suc[1(S)-(2H-tetrazolyl-5-ylmethyl)amino]-Trp-Phe- [(R)-NH-CH(CH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>)-CH<sub>2</sub>-NH] - } trifluoroacetic acid

(ah) Cyclo{ -Suc[1(S)-(morpholin-4-yl)]-Trp-Phe- [(R)-NH-CH(CH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>)-CH<sub>2</sub>-NH] - } trifluoroacetic acid

*03*  
*Conclude*

(ai) Cyclo{-Suc[1(S)-N(CH<sub>3</sub>)<sub>2</sub>]-Trp-Phe-[ (R) -NH-CH(CH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>) -CH<sub>2</sub>-NH] -} trifluoroacetic acid

(aj) Cyclo{-Suc[1(S)-(piperidin-4-yl)-Trp-Phe-[ (R) -NH-CH(CH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>) -CH<sub>2</sub>-NH] -} trifluoroacetic acid

(ak) Cyclo{-Suc[1(S)-(N(CH<sub>2</sub>CH<sub>2</sub>OH)<sub>2</sub>)]-Trp-Phe-[ (R) -NH-CH(CH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>) -CH<sub>2</sub>-NH] } trifluoroacetic acid

(al) Cyclo{-Suc[1(S)-(N(CH<sub>2</sub>CH(OH)CH<sub>2</sub>OH)]-Trp-Phe-[ (R) -NH-CH(CH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>) -CH<sub>2</sub>-NH] -} trifluoroacetic acid

(am) Cyclo{-Suc[1(S)-(3-carboxypropanoyl)amino]-Trp-Phe-[ (R) -NH-CH(CH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>) -CH<sub>2</sub>-NH] -}

(an) Cyclo{-Suc[1(S)-[3-N'- $\beta$ -D-glucopyranos-1-yl)-carboxamidopropanoyl]amino]-Trp-Phe-[ (R) NH-CH(CH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>) -CH<sub>2</sub>NH] -}

(ao) Cyclo{-Suc[1(S)-[(carboxymethyl)amino]-Trp-Phe-[ (R) -NH-CH(CH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>) -CH<sub>2</sub>-NH] -} trifluoroacetic acid

(ap) Cyclo{-Suc[1(S)-[N'- $\beta$ -D-glucopyranos-1-yl)-carboxamideomethyl]amino]-Trp-Phe-[ (R) -NH-CH(CH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>) -CH<sub>2</sub>-NH] -} trifluoroacetic acid

(aq) Cyclo{-Suc[1(S)-(quinyl)amine]-Trp-Phe-[ (R) -NH-CH(CH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>) -CH<sub>2</sub>-NH] -}

(ar) Cyclo{-Suc[1(S)-(4-aminobutanoyl)amino]-Trp-Phe-[ (R) -NH-CH(CH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>) -CH<sub>2</sub>-NH] -} trifluoroacetic acid

(as) Cyclo{-Suc[1(S)-[1,4']bipiperidin-1-yl]acetamido]-Trp-Phe-[ (R) -NH-CH(CH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>) -CH<sub>2</sub>-NH] -} trifluoroacetic acid

(at) Cyclo{-Suc[1-N-( $\beta$ -D-glucopyranos-1-yl)-carboxamido]-Trp-Phe-[ (R) -NH-CH(CH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>) -CH<sub>2</sub>-NH] -}

(au) Cyclo{-Suc[1(S)-[N'- (2-N-acetyl- $\beta$ -D-glucopyranos-1-yl)-carboxyamido]-Trp-Phe-[ (R) -NH-CH(CH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>) -CH<sub>2</sub>-NH] -} .

*04*

5. (Amended three times) A composition comprising a compound of formula (I) according to Claim 1 in combination with a suitable carrier or excipient.

*PS*

8. (twice amended) A method of inhibiting bronchoconstriction comprising administering a compound according to Claim 7 for a time and under conditions effective to treat the bronchospastic and inflammatory component of asthma, coughing, pulmonary irritation, intestinal spasms, spasms of the biliary tract, local spasms of the bladder and of the ureter during cystitis, kidney infections and colics.

*PS*

9. (twice amended) A method of inhibiting bronchoconstriction comprising administering a compound according to Claim 7 for a time and under conditions effective to produce an anxiolytic effect.

*Q7*

14. (amended three times) A method of inhibiting bronchoconstriction comprising administering quantities of between 0.02 and 10 mg/kg of body weight of active principle consisting of a compound of formula(I), according to Claim 1, to a patient afflicted with asthma, coughing, pulmonary irritation, intestinal spasms, spasms of the biliary tract, local spasms of the bladder and of the uterter during cystitis, and kidney infections and colics for a time and under conditions effective to antagonize NK-2 receptors.